IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Marc Karel Jozef Francois	Confirmation No: 1592
Serial No.	:	10/585,754	Art Unit: 1624
Filed	:	July 12, 2006	Examiner: Adam C. Milligan
For	:	MITRATAPIDE ORAL SOLUTION	

REPLY BRIEF UNDER 37 CFR § 41.41

This Reply Brief is in response to the Examiner's Answer of May 13, 2011. Since this paper is being filed on or before July 13, 2011, it is timely. In addition to the arguments set forth in the Second Appeal Brief of February 23, 2011, Appellants submit that the Examiner's rejection is in error for the following reasons.

I. The Examiner Improperly Relies Upon Appellants' Disclosure In Support Of The Rejection

As explained in the Second Appeal Brief, not every pharmaceutically acceptable solvent will meet the solubility requirement of claim 1 (*Id.* at 5). Appellants also noted that the Examiner had not addressed this claim feature in the rejection (*Id.* at 9).

The Examiner now attempts to account for this claim feature by relying upon Appellants' own disclosure:

> With regard to the recitation of a "a pharmaceutically acceptable solvent wherein mitratapide has a solubility of 5mg/ml or higher", it is noted that the instant specification states that "[tlhe pharmaceutically acceptable solvent wherein mitratapide has a solubility of 5 mg/ml or higher is preferably selected from the group consisting of ...polyethyleneglycol 400" (Instant specification at p.3, lines 31 -36, ¶12).

(Examiner's Answer at 7). The Examiner's reliance upon the present specification for this purpose is improper.

Appellants' argument relating to solubility relied upon Table 1 of the specification (Second Appeal Brief at 5) which reads:

[0013] The solubility of mitratapide in different pharmaceutical solvents was measured at room temperature of about 22° C. and listed in Table 1.

TABLE 1

solubility of mitratapide in mg/ml

Solvent	solubility (mg/ml)
glycerol	<0.02*
sesame oil	<0.05
caprylic/capric acid triglyceride (Miglyol 812 ®)	<5
caprylic/capric/succinic acid triglyceride (Miglyol 829 ®)	<5
caprylidecapridilmoleic acid triglyceride (Miglyol 818 ®)	<5
apricot Kernel oil PEG-6 complex (Labrafil 1944CS ®)	<5
corn oil PEG-6 complex (Labrafil 2125CS ®)	<5
caprylic/capric diester of propylene glycol	<5
propyleneglycol	2.2*
dimethyl isosorbide (2,5-di-O-methyl-1,4:3,6-dianhydro D-glucitol)	>5
diethylene glycol monoethyl ether (Transcutol ®)	>5
caprylocaproyl-8 glyceride (Labrasol ®)	>5
Dropylene glycol monolaurate (Lauroglycol ®)	>5
polyethyleneglycol 400 (PEG 400)	24.8*

*per g solution

As seen, Table 1 provides evidence that not every pharmaceutical solvent provides the solubility feature of claim 1.

The Examiner has failed to identify any disclosure of this type in the prior art, and has impermissibly used Appellants' own disclosure to account for the solubility feature of claim 1. This is clear evidence of the impermissible hindsight that the Examiner has used in making the obviousness rejection.

II. The Examiner Has Not Performed The Analysis Required By The *Jones* And *Baird* cases

Appellants noted in their Appeal Brief that it was error for the Examiner to select mitratapide from the thousands of active agents disclosed in Heeres without performing the analysis required by *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992) and *In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994) as to why a person of ordinary skill would have made this selection (Second Appeal Brief at 7). In response, the Examiner states that

mitratapide is one of the "140 or so" compounds whose structure is specifically disclosed by Heeres. (Examiner's Answer at 9.).

However, the possibility that mitratapide is a compound whose structure is specified by Heeres is legally irrelevant, as Heeres describes a vast genus of active agents. The present specification acknowledges that mitratapide is described as compound 40 in Heeres and is useful as a lipid lowering agent (*Id.*, [0003]). Not acknowledged by the Examiner, however, is that Heeres sets forth data that was obtained by testing a number of the described active agents for inhibition of apolipoprotein B ("apo B") (*Id.*, Example 7), and that the data reported in Table 13 of Heeres shows that mitratapide (compound 40) does not exhibit the best IC_{50} value. Thus, when Heeres is considered as a whole, without knowledge of the present disclosure and claims, one can see that the Examiner's convenient selection of mitratapide from Heere's vast genus of active agents is based upon impermissible hindsight.

III. The Examiner Continues To Improperly Apply Basit

Appellants noted that Basit clearly teaches away from using PEG 400 as a solvent for the active agents used in Heeres because PEG 400 can reduce gastrointestinal transit time and, thus, reduce bioavailability (Second Appeal Brief at 8-9).

In response, however, the Examiner doesn't dispute that Basit teaches away from using PEG 400. Rather, the Examiner contends that his point in citing Basit was simply to support the proposition that PEG 400 is not a "completely inert" pharmaceutical excipient:

> Basit cautions that for some drugs that are absorbed predominantly in the small intestine, the decreased small intestinal transit time may limit the opportunity for drug absorption, and thus the point of Basit is that PEG 400 cannot be considered a completely inert pharmaceutical excipient.

(Examiner's Answer at 10). According to the Examiner, a person of ordinary skill and aware that PEG 400 was not "completely inert" would have been motivated to use it with

one of the numerous active agent that Heeres describes simply because Heere allegedly teaches that PEGs generally find use as solubilizing agents:

> Given that Basit teaches PEG 400 is a well known solubilizing agent and Heeres teaches the use of PEG, generally, for solubilizing active ingredients, it would have been obvious to choose PEG 400 as the specific PEG when formulating the composition of Heeres.

(*Id.*).

The Examiner, however, does not identify any disclosure in Heeres supporting the assertion that Heeres "teaches the use of PEG generally, for solubilizing active ingredients." In fact, it appears that Heeres, at best, only describes the use of solubilizing agents in general and, even then, only in conjunction with parenteral formulations, not oral formulations (*Id.*, 10:16-18). Thus, the Examiner's position lacks factual support.

In sum, there is no dispute that Basit teaches away from using PEG 400 as a solvent, and no support for using Basit in the manner that the Examiner has proposed.

IV. The Examiner Has Not Responded To Appellants' Arguments Concerning The Unpredictability Of This Art Area

Appellants have noted that Basit's disclosure that PEG 400 may reduce gastrointestinal transit time (and thus, bioavailability) of the active establishes that this art area is unpredictable (Second Appeal Brief at 8). The Examiner has not responded to this issue. This failure to respond constitutes an admission that the art area is unpredictable.

Conclusion

For the reasons set forth in the Second Appeal Brief and above, the Examiner's rejection under 35 U.S.C. § 103(a) is in error. Appellants respectfully ask the Board to reverse the rejection.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment in connection herewith to Deposit Account No. 10-0750/PRD2166USPCT/JKM.

Respectfully submitted,

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